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10/565,831	01/25/2006	Junya Toguchida	Q92863	6132

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EXAMINER	
FRAZIER, BARBARA S	
ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
11/18/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/565,831	TOGUCHIDA, JUNYA	
	Examiner	Art Unit	
	BARBARA FRAZIER	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11 and 20-36* is/are pending in the application.

4a) Of the above claim(s) *29-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,20-28,35 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/10/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 11 and 20-36 are pending in this application. Claims 1-10 and 12-19 stand canceled.

2. Claims 29-34 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/27/08.

3. Claims 11, 20-28, 35, and 36 are examined.

Rejections Withdrawn

4. The rejection of claims 11, 20-28, 35, and 36 under 35 U.S.C. 103(a) as being unpatentable over Paralkar (EP 1205189) in view of Tani et al (Bioorganic and Medicinal Chemistry, Vol. 10, pp. 1107-1114, 2002) and Fortier et al (J. Bone Joint Surg., Vol. 84-B, pp. 276-288, 2002) is withdrawn in view of Applicant's amendments to claims 11, 26, and 35.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. **Claims 11 and 20-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.** The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Independent claims 11 and 26, as amended, are now drawn to methods for treating cartilage-related diseases which consists of administering a composition consisting of a substance having an EP2 agonist activity (claim 11) or consisting of a substance having an EP2 agonist activity and a second substance (claim 26). While the specification provides support for a composition consisting of the elected species, (5Z, 9β, 11α, 13E)-17,17-propano-11,16-dihydroxy-9-chloroprosta-5,13,19-trienoic acid (see Example 2 and Figure 4), the specification does not provide support for the broad genus of any substance having an EP2 agonist activity as an active ingredient. Instead, the specification teaches a method for treating cartilage-related disease which **comprises** administering a composition which **comprises** as an active ingredient a substance having an EP2 agonist activity (for example, see page 3, lines 31-32 and page 5, lines 4-5), and that the remedy of the present invention may be administered as a combined preparation, and especially may be used with medicaments for treating other bone diseases (see page 63, lines 4-10). The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., *Mars Inc. v. H.J.*

Heinz Co., 377 F.3d 1369, 1376, 71 USPQ2d 1837, 1843 (Fed. Cir. 2004) On the other hand, the transitional phrase "consisting of" excludes any element, step, or ingredient not specified in the claim. *In re Gray*, 53 F.2d 520, 11 USPQ 255 (CCPA 1931); *Ex parte Davis*, 80 USPQ 448, 450 (Bd. App. 1948) ("consisting of" defined as "closing the claim to the inclusion of materials other than those recited except for impurities ordinarily associated therewith."). See MPEP 2111.03. Therefore, the new limitations of a method for treating cartilage-related disease, which **consists** of administering a composition **consisting** of a substance having an EP2 agonist activity, constitute new matter.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 11 and 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cameron et al (WO 98/27976, previously cited by Applicants in the IDS filed 4/28/06), alone or further in view of Anastassiades (US Patent 6,133,230, previously cited by Applicants in the IDS filed 1/25/06).

The claimed invention is drawn to a method for treating cartilage-related disease, which consists of administering a composition to a subject in need of stimulating

chondrocyte growth, said composition consisting of a substance having an EP2 agonist activity as an active ingredient for treating cartilage-related disease and a pharmaceutically acceptable carrier.

Cameron et al teach methods for treating a mammal having a condition which present with low bone mass or other skeletal disorders comprising administering to a mammal a therapeutically effective amount of an EP2 receptor subtype agonist (abstract). The conditions to be treated include osteoporosis, bone fractures, osteotomy, vertebral synostosis (page 3, lines 20-26). Conditions such as osteoporosis, repair and healing of bone fractures, and bone deformation are cartilage-related diseases, as evidenced by Applicant's specification (page 7, lines 4-23). The compounds are generally administered in the form of a pharmaceutical composition comprising at least one of the compounds of the invention together with a pharmaceutically acceptable vehicle or diluent (page 80, lines 1-5).

While Cameron et al do not specifically teach that the subject to be treated is in need of stimulating chondrocyte growth, Cameron et al do teach that the mammal to be treated may present with low bone mass or other skeletal disorders (abstract) and that the compound used may be applied to the cartilage growth plate (page 79, lines 5-6), and therefore one skilled in the art would reasonably expect that the subject would be in need of stimulating chondrocyte growth in order to form new bone tissue.

Additionally or alternatively, Anastassiades teaches that exogenous prostaglandin E may suppress the cartilage damage and degeneration caused by IL-1 (see col. 1, line 65 - col. 2, line 3). Thus, it would have been obvious to a person having

ordinary skill in the art at the time the invention was made to administer a substance having EP2 agonist activity to a subject in need of stimulating chondrocyte growth, since an EP2 agonist would be expected to perform similarly to exogenous prostaglandin E in suppressing cartilage damage and degeneration, thus allowing for chondrocyte growth.

Regarding claim 20, one skilled in the art would reasonably expect that the treatment of a cartilage-related disease, such as osteoporosis, would include treatment of the cartilage disorder associated with said disease. Additionally or alternatively, Anastassiades teaches that exogenous prostaglandin E may suppress the cartilage damage and degeneration caused by IL-1 (see col. 1, line 65 - col. 2, line 3). Therefore, one skilled in the art would reasonably expect a compound which behaves similarly to exogenous prostaglandin E, such as an EP2 agonist, to also suppress cartilage damage and degeneration, and thus would treat the cartilage disorder related to said cartilage-related disease.

Regarding the effects of the EP2 agonist (claims 21-25), one skilled in the art would reasonably expect the compounds of Cameron et al to have the same effects, since the same compounds are administered to the same population.

9. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cameron et al (WO 98/27976) alone or further in view of Anastassiades (US Patent 6,133,230) as applied to claims 11 and 20-25 above, and optionally further in view of Fortier et al (J. Bone Joint Surg., Vol. 84-B, pp. 276-288, 2002, previously cited).

Claims 26 of the claimed invention is drawn to a method for treating cartilage-related disease, which consists of administering a composition to a subject in need of stimulating chondrocyte growth, said composition consisting of (a) a substance having an EP2 agonist activity and (b) one or more substances selected from transforming growth factor-B, insulin-like growth factor, basic fibroblast growth factor, epidermal growth factor, growth hormone and platelet-derived growth factor, as active ingredients for treating cartilage-related disease, and a pharmaceutically acceptable carrier.

The invention of the combined references is delineated above (see paragraph 7). Anastassiades further teach that IGF-1 or TGF-β may be administered with a prostaglandin in amounts effective to promote the production of chondrocyte matrix or prevent the degeneration of the chondrocyte matrix (col. 2, lines 32-49).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to add IGF-1 or TGF-β to the compound of Cameron et al to treat a cartilage-related disease such as osteoporosis or bone fracture; thus arriving at the claimed invention. One skilled in the art would be motivated to do so, with a reasonable expectation of success, because the addition of IGF-1 or TGF-β to a prostaglandin results in the benefits of promoting the production of chondrocyte matrix or preventing the degeneration of the chondrocyte matrix, as taught by Anastassiades, and therefore one skilled in the art would reasonably expect that the addition of IGF-1 or TGF-β to a compound which behaves similarly to a prostaglandin, i.e., a substance having EP2 agonist activity, would also result in promoting the production of chondrocyte matrix or preventing the degeneration of the chondrocyte matrix.

Additionally or alternatively, Fortier et al teach that the addition of IGF-1 to chondrocyte grafts enhanced chondrogenesis in cartilage defects, including incorporation into surrounding cartilage, and the IGF-1 improves the repair capabilities of chondrocyte-fibrin grafts in large full-thickness repair models (abstract).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to add IGF-1 to the compound of Cameron et al to treat a cartilage-related disease such as osteoporosis or bone fracture; thus arriving at the claimed invention. One skilled in the art would be motivated to do so, with a reasonable expectation of success, because the addition of IGF-1 provides the benefits of enhanced chondrogenesis in cartilage defects and improved repair capabilities of chondrocyte-fibrin grafts, as taught by Fortier et al, which one would desire when treating a cartilage-related disease such as osteoporosis or bone fracture.

10. Claims 27, 28, 35, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cameron et al (WO 98/27976) alone or further in view of Anastassiades (US Patent 6,133,230) as applied to claims 11 and 20-25 above, and further in view of Tani et al (US Patent 6,110,969, previously cited by Applicants in the IDS filed 4/28/06).

Claims 27 and 28 are drawn to the method according to claim 11, wherein the substance having an EP2 agonist activity is one or more compounds; Applicants have elected (5Z, 9β, 11α, 13E)-17,17-propano-11,16-dihydroxy-9-chloroprosta-5,13,19-trienoic acid as the elected species. Claims 35 and 36 are drawn to a method for

treating cartilage-related disease, which consists of administering a composition consisting of a substance, as an active ingredient, having an EP2 agonist activity selected from a compound; Applicants have elected (5Z, 9β, 11α, 13E)-17,17-propano-11,16-dihydroxy-9-chloroprosta-5,13,19-trienoic acid as the elected species.

The invention of the combined references is delineated above (see paragraph 7).

The invention of the combined references does not specifically teach that the substance having EP2 agonist activity is (5Z, 9β, 11α, 13E)-17,17-propano-11,16-dihydroxy-9-chloroprosta-5,13,19-trienoic acid.

Tani et al teach cycloalkyl-prostaglandin E2 derivatives which can strongly bind on EP2 subtype receptor, and therefore are useful for prevention and/or treatment of abnormal bone formation (abstract). Tani et al exemplify the compound (5Z, 9β, 11α, 13E)-17,17-propano-11,16-dihydroxy-9-chloroprosta-5,13,19-trienoic acid (see Example 17(1), column 94).

It would have been obvious to a person having ordinary skill in the art at the time the invention was made to selected (5Z, 9β, 11α, 13E)-17,17-propano-11,16-dihydroxy-9-chloroprosta-5,13,19-trienoic acid as the substance having EP2 receptor activity in the methods of the invention of the combined references; thus arriving at the claimed invention. One would be motivated to do so because said species is already known to strongly bind to EP2 receptor, and therefore one skilled in the art would reasonably expect said species to be suitable for the method of Cameron et al, absent evidence to the contrary. One would reasonably expect success from the use of the species of Tani

et al with the method of Cameron et al because both references are drawn to treatment of abnormal bone formation using a substance having EP2 agonist activity.

Conclusion

No claims are allowed at this time.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BARBARA FRAZIER whose telephone number is (571)270-3496. The examiner can normally be reached on Monday-Thursday 9am-4pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BSF

/David J Blanchard/
Primary Examiner, Art Unit 1643